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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,064	08/02/2005	Pierre Michel Desmons	B45308	4877

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EXAMINER	
GANGLE, BRIAN J	
ART UNIT	**PAPER NUMBER**
1645	
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05/14/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/529,064	DESMONS ET AL.	
	Examiner	Art Unit	
	Brian J. Gangle	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-15* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10 and 15* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 2/15/2007 has been entered.

The amendment and remarks, filed 2/15/2007, are acknowledged. Claim 2 has been amended. Claims 1-15 are pending. Claims 11-14 are withdrawn as being drawn to non-elected inventions. Claims 1-10 and 15 are currently under examination.

Claim Rejections Withdrawn

The rejection of claim 2 under 35 U.S.C. 112, second paragraph, as being indefinite because of the term "prevalent," is withdrawn in light of applicant's amendment thereto.

Claim Rejections Maintained

35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

The rejection of claims 1-9, and newly submitted claim 15, under 35 U.S.C. 102(b) as being anticipated by Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That while Berthet teach multivalent bleb preparations, they do not teach a composition comprising blebs that are deficient in PorA in combination with blebs that are not deficient in PorA.

2. That the disclosure of CU-385 and H44/76, by Berthet, is not made in reference to a bleb preparation with blebs from both of these strains, but rather to a single bleb preparation that is immunoprotective against both of these strains.

3. That Berthet does not inherently disclose a composition comprising blebs that are deficient in PorA in combination with blebs that are not deficient in PorA because Berthet discloses combinations of serotypes that, while they do contain the strains CU-385 and H44/76 (which are deficient PorA and not deficient in PorA, respectively), these serotypes may contain other strains which do not have the same PorA content as CU-385 and H44/76. Therefore, the composition of Berthet does not necessarily and/or inevitably contain at least one bleb preparation that is deficient in PorA in combination with at least one bleb preparation that is not deficient in PorA.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1-3, on page 36, Berthet discloses vaccine bleb preparations which contain a mixture of blebs from several subtype/serotypes, such as P1.15 and P1.7,16. Applicant is correct that, on page 35, Berthet refers to compositions that should be immunoprotective against strains CU-385 and H44/76. However, it is not accurate to state that said immunoprotective preparation is not a mixture. Berthet refers to the manufacture of a bleb vaccine that is produced using more than one process in order to optimize the preparation. This suggests that said vaccine contains a mixture, especially since the vaccine should be protective against multiple strains. Additionally, Berthet refers to vaccines containing blebs from multiple serotypes, including P1.15 and P1.7,16. While there are strains in addition to CU-385 and H44/76, which are encompassed by these serotype designations, the skilled artisan reading Berthet would clearly realize that vaccines containing blebs from multiple serotypes, including P1.15 and P1.7,16 should contain blebs from strains CU-385 and H44/76, since Berthet states that vaccines should be immunoprotective against these two strains. Moreover, applicant explicitly recognized that Berthet discloses combinations of blebs from strains H44/76 and CU-385 on page 11, lines 29-33 of the instant specification. The fact that Berthet does not mention the PorA content of these strains is not relevant, as CU-385 is deficient in PorA and H44/76 is not deficient in PorA.

As stated previously, the instant claims are drawn to a multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76 (claim 1). Further limitations found in dependent claims include the composition of claim 1 wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype that is selected from the most, second, third, or fourth most prevalent in a country of use (claims 2 and 15); wherein the bleb preparation deficient in PorA has less than 22% PorA of total bleb protein, or lacks PorA (claim 3); wherein the bleb preparation not deficient in PorA has more than 28% PorA of total bleb protein (claim 4); and wherein the bleb preparation deficient in PorA is derived from the meningococcal CU-385 strain (claim 5). The instant claims further include a vaccine for the treatment of neisserial disease comprising the multivalent meningococcal bleb composition of claim 1 and a pharmaceutically acceptable excipient (claim 6). Further limitations found in dependent claims include the vaccine of claim 6 additionally comprising one or more plain or conjugated meningococcal capsular polysaccharides selected from the following list of serogroups: A, C, Y and W (claim 7); wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1.4 (claim 8); and wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1 .7,16 (claim 9).

Berthet *et al.* disclose a multivalent vaccine comprising mixtures of meningococcus bleb preparations as well as a pharmaceutically acceptable excipient (see page 36, lines 5-28 and page 33, lines 1-5). Said vaccine comprises mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4 (see page 36, lines 15-19). Said vaccine is also disclosed as comprising any or all of the capsular polysaccharides A, C, Y, or W (see page 36, lines 11-14). It should be noted that applicant discloses, in the instant specification, that P1.15 is the serosubtype of strain CU-385, which has 20% PorA (see page 22, lines 19-22 and page 24, lines 8-11) and that P1.7,16 is the serosubtype of strain H44/76, which has 30% PorA (see page 6, line 18 and page 25, table 1). Additionally, applicant acknowledges in the instant specification on page 11, lines 29-33, that Berthet discloses combinations of blebs from strains

H44/76 and CU-385. Therefore, the disclosure of Berthet *et al.* anticipates the instantly claimed invention.

The rejection of claims 1-9 under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Granoff *et al.* (PCT Publication WO 02/09643, 2/7/2002), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That the examiner is incorrect in asserting that Granoff discloses vaccines that contain blebs from multiple strains of *Neisseria* and that Granoff discloses the "Norwegian vaccine" and mixtures containing blebs from strain CU-385.

2. That Granoff's disclosure of the Norwegian vaccine refers to a preparation containing blebs from a single strain of *Neisseria*.

3. That Granoff's reference to CU-385 is limited to its use in testing the sera of animals immunized with the CHORI vaccine.

4. That Figure 1 does not disclose strain CU-385, but only a strain of serosubtype P1.15, which includes strains other than CU-385.

5. That the examiner incorrectly asserts that Granoff discloses individual bleb vaccines that comprise CU-385, and that Figure 1 only discloses a strain of serosubtype P1.15, not CU-385.

6. That Granoff does not disclose any compositions containing mixtures that include blebs of serosubtype P1.15, much less CU-385. Applicant further argues that claims 1-9 are not drawn to mixtures of blebs from different strains, but to mixtures containing blebs that are deficient in PorA and blebs that are not deficient in PorA.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1 and 2, contrary to applicant's assertion, it is clear that Granoff discloses vaccines containing blebs from multiple strains of *Neisseria* (see, for example, page 7, line 28 through page 8, line 12). It is also clear that Granoff discloses the Norwegian vaccine (page 5, lines 5-10). The examiner has not asserted that mixtures containing the Norwegian vaccine are disclosed.

Regarding arguments 1 and 3, applicant is correct that the discussion of CU-385 on pages 44 and 48 are in reference to the use of CU-385 in testing antisera, and that these pages do not disclose a mixture containing CU-385. However, this does not mean that Granoff lacks disclosure of CU-385, or that a combination of CU-385 with the Norwegian vaccine would be unobvious. Both a composition containing CU-385 and one containing H44/76 are disclosed as effective vaccines. According to MPEP 2144.06, "It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980).

Regarding arguments 4 and 5, Figure 1 discloses a vaccine with the serosubtype B:4:P1.15, that was used in Cuba and Brazil from 1987-1991. Granoff, on page 14, refers to an OMV vaccine prepared by the Finley Institute in Cuba which has been given to millions of children in South America. It is clear from an examination of the art and the instant specification, that CU-385 (commonly referred to as the Cuban strain) is the strain referred to in Granoff on page 14 and in Figure 1.

Regarding argument 6, as stated previously, Granoff discloses vaccine compositions which contain a mixture of blebs from different strains. Granoff also discloses vaccines that individually comprise CU-385 and H44/76 (the Norwegian vaccine). While Granoff does not explicitly disclose the combination blebs from these two strains, it would have been obvious to combine them for the reasons previously set forth. It is understood that the claimed invention is not merely a combination of blebs from different strains, but of a combination of blebs that are deficient in PorA and blebs that are not deficient in PorA; however, the combination of CU-385 and H44/76 meets this limitation.

As stated previously, the instant claims are drawn to a multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76 (claim 1). Further limitations found in dependent claims include the composition of claim 1 wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a

serosubtype that is the most, second, third, or fourth most prevalent in a country of use (claim 2); wherein the bleb preparation deficient in PorA has less than 22% PorA of total bleb protein, or lacks PorA (claim 3); wherein the bleb preparation not deficient in PorA has more than 28% PorA of total bleb protein (claim 4); and wherein the bleb preparation deficient in PorA is derived from the meningococcal CU-385 strain (claim 5). The instant claims further include a vaccine for the treatment of neisserial, preferably meningococcal, disease comprising the multivalent meningococcal bleb composition of claim 1 and a pharmaceutically acceptable excipient (claim 6). Further limitations found in dependent claims include the vaccine of claim 6 additionally comprising one or more plain or conjugated meningococcal capsular polysaccharides selected from the following list of serotypes: A, C, Y and W (claim 7); wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1.4 (claim 8); and wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1 .7,16 (claim 9).

Granoff *et al.* disclose an outer membrane vesicles (bleb) vaccine that comprises a mixture of blebs from genetically diverse strains of *Neisseria meningitidis* as well as a pharmaceutically acceptable excipient (see page 6, lines 23-31 and page 22, lines 5-20). Granoff *et al.* also disclose a bleb vaccine that contains a mixture of blebs from a serogroup C strain as well as a strain with the serogroup P1.4 (see page 7, lines 19-27). Granoff *et al.* further disclose individual bleb vaccines that each comprise strains with the serosubtypes P1.15 (CU-385) and P1.7,16 (see figure 1). Additionally, Granoff *et al.* disclose that the disclosed mixture vaccine has the advantage of broad spectrum protective immunity (see page 15, lines 10-12). It should be noted that applicant discloses, in the instant specification, that P1.15 is the serosubtype of strain CU-385, which has 20% PorA (see page 22, lines 19-22 and page 24, lines 8-11) and that P1.7,16 is the serosubtype of strain H44/76, which has 30% PorA (see page 6, line 18 and page 25, table 1).

Granoff *et al.* do not explicitly disclose that the bleb vaccine mixture should contain strains with serosubtypes P1.15 (CU-385) and P1.7,16.

However, it would have been *prima facie* obvious to a person of ordinary skill in the art at the time of invention to use the strains with serosubtypes P1.15 (CU-385) and P1.7,16 in the mixture of the bleb vaccine in order to obtain the advantage of broad spectrum protective

immunity, as disclosed by Granoff *et al.* Therefore, the use of the serosubtypes P1.15 (CU-385) and P1.7,16 in the mixture of the bleb vaccine is deemed an obvious variation of the disclosed composition.

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-10 under 35 U.S.C. 103(a) as being unpatentable over Berthet *et al.* (PCT Publication WO 01/09350, 2/8/2001) in view of Lehmann *et al.* (APMIS 99:769-772, 1991), is maintained for the reasons set forth in the previous office action.

Applicant argues:

1. That, as discussed above, Berthet does not teach compositions that contain at least one bleb preparation that is deficient in PorA in combination with at least one bleb preparation that is not deficient in PorA.

2. That Berthet does not teach any vaccine compositions containing the strain CU-385.

3. That the examiner has relied on the instant specification for the teaching that CU-385 is deficient in PorA, which constitutes improper hindsight reasoning.

4. Lehman does not remedy any of the above failings.

Applicant's arguments have been fully considered and deemed non-persuasive.

Regarding arguments 1 and 2, as discussed above, it is clear from reading Berthet, that vaccines containing blebs from multiple strains are disclosed; and that strains CU-385 and H44/76 have been contemplated. Moreover, applicant explicitly recognized that Berthet discloses combinations of blebs from strains H44/76 and CU-385 on page 11, lines 29-33 of the instant specification.

Regarding arguments 3 and 4, the examiner has not relied upon any teachings in the instant specification for to provide reasons for combining references. The examiner is simply using the instant specification to point out that applicant regards CU-385 as a strain that is deficient in PorA. This is an inherent property of the strain, not a judgment made using hindsight reasoning. Furthermore, it is not required that it be recognized whether the compositions of the prior art contained a specific amount of PorA, only that the compositions actually contained the appropriate amounts. Therefore, it is not relevant whether it was recognized that CU-385 is deficient in PorA, or that H44/76 is not deficient in PorA. The fact that these strains had this characteristic means that any composition comprising blebs from these strains would necessarily meet the limitations of the instant claims. In addition, the test for obviousness is what the combined teachings of the references would have suggested to one of ordinary skill in the art, and there is no requirement that the examiner have the same reasons for combining as applicant. As stated previously, it is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). One would have had a reasonable expectation of success based on the success already shown with each of the components of the composition.

As stated previously, the instant claims are drawn to a multivalent meningococcal bleb composition comprising a bleb preparation deficient in PorA in that it has less than 80% of the amount of PorA as compared to the same quantity of blebs made from strain H44/76 and a bleb preparation that is not deficient in PorA compared to blebs made from strain H44/76 (claim 1). Further limitations found in dependent claims include the composition of claim 1 wherein the

bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serotype that is most, second, third, or fourth most prevalent in a country of use (claim 2); wherein the bleb preparation deficient in PorA has less than 22% PorA of total bleb protein, or lacks PorA (claim 3); wherein the bleb preparation not deficient in PorA has more than 28% PorA of total bleb protein (claim 4); and wherein the bleb preparation deficient in PorA is derived from the meningococcal CU-385 strain (claim 5). The instant claims further include a vaccine for the treatment of neisserial, preferably meningococcal, disease comprising the multivalent meningococcal bleb composition of claim 1 and a pharmaceutically acceptable excipient (claim 6). Further limitations found in dependent claims include the vaccine of claim 6 additionally comprising one or more plain or conjugated meningococcal capsular polysaccharides selected from the following list of serotypes: A, C, Y and W (claim 7); wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1.4 (claim 8); wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1 .7,16 (claim 9); and wherein the bleb preparation that is not deficient in PorA is derived from a meningococcal strain with a serosubtype of P1.16 (claim 10).

Berthet *et al.* disclose a multivalent vaccine comprising mixtures of meningococcus bleb preparations as well as a pharmaceutically acceptable excipient (see page 36, lines 5-28 and page 33, lines 1-5). Said vaccine comprises mixtures of bleb preparations from 2 or more strains, including serotypes P1.15, P1.7,16, and P1.4 (see page 36, lines 15-19). Said vaccine is also disclosed as comprising any or all of the capsular polysaccharides A, C, Y, or W (see page 36, lines 11-14). Applicant discloses in the instant specification that P1.15 is the serosubtype of strain CU-385, which has 20% PorA (see page 22, lines 19-22 and page 24, lines 8-11). Applicant also discloses that P1.7,16 is the serosubtype of strain H44/76, which has 30% PorA (see page 6, line 18 and page 25, table 1).

Berthet *et al.* differs from the instant application in that they do not disclose the use of serosubtype P1.16 in the vaccine composition.

Lehmann *et al.* disclose an outer membrane vesicle (bleb) vaccine comprising blebs from a meningococcal strain with the serosubtype P1.16 (see abstract).

"It is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition to be used for the very same purpose.... [T]he idea of combining them flows logically from their having been individually taught in the prior art." In re Kerkhoven, 626 F.2d 846, 850, 205 USPQ 1069, 1072 (CCPA 1980). Therefore, it would have been obvious to one of ordinary skill in the art to use blebs from a meningococcal strain with the serosubtype P1.16 in the vaccine composition of Berthet *et al.*

New Claim Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 6-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for multivalent vaccines providing protection against *Neisseria meningitidis*, does not reasonably provide enablement for multivalent vaccines for the treatment of neisserial disease. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(A)). These include: nature of the invention, breadth of the claims, guidance of the specification, the existence of working examples, state of the art, predictability of the art and the amount of experimentation necessary.

In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970) states, "The amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability in the art." "The "amount of guidance or direction" refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable

the art is, the less information needs to be explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as to how to make and use the invention in order to be enabling" (MPEP 2164.03). The MPEP further states that physiological activity can be considered inherently unpredictable. Thus, Applicant assumes a certain burden in establishing that inventions involving physiological activity are enabled. All of the Wands factors have been considered with regard to the instant claims, with the most relevant factors discussed below.

Nature of the invention: The instant claim is drawn to multivalent meningococcal bleb vaccines for the treatment of neisserial disease. Said vaccines contain blebs that are deficient in PorA and blebs that are not deficient in PorA, relative to blebs from strain H44/76.

Breadth of the claims: The claim encompasses treatment and prevention of all diseases caused by bacteria of the genus *Neisseria.* This includes meningitis (caused by *Neisseria meningitidis*), gonorrhea (caused by *Neisseria gonorrhoeae*), and opportunistic infections caused by other species within the genus.

Guidance of the specification/The existence of working examples: The specification does not disclose any challenge experiments with any bleb compositions, either to show prevention or treatment of any neisserial disease. The specification does refer to work in the art with the so-called Norwegian and Cuban vaccine strains, as well as a New Zealand strain.

State of the art: The Norwegian and Cuban strains are accepted to be effective in preventing meningitis caused by *Neisseria meningitidis* (Granoff *et al.*, WO 02/09643; Lehmann *et al.*, APMIS 99:769-772, 1991; Rodriguez *et al.*, Mem Inst. Oswaldo Cruz, 94:433-440, 1999). There is no evidence in the art that a vaccine containing antigens from *Neisseria meningitidis* would have any effect whatsoever on diseases caused by other bacteria in the genus *Neisseria.* Further, regarding treatment of neisserial disease, while the vaccines in the art have been shown to be protective, there is no evidence that they would be capable of treating established disease. The claimed treatment is not a method that uses a product with antimicrobial properties, but is a treatment that requires administration of an antigenic substance which would stimulate the immune system respond to the pathogen. The humoral immune response (which would be induced by the claimed vaccine) requires time to build. As evidenced by Abbas *et al.* (Cellular and Molecular Immunology, 5th ed., 2005, pages 190-191), the primary antibody response does

not occur for 5-10 days after immunization. However, the onset of neisserial meningitis is sudden, with a rapid progression of the illness, leasing to permanent damage to the central nervous system or death within hours (Filippis *et al.*, Diag. Microbiol. Infect. Dis., 51:85-90, 2005). This hardly provides time for an immune response to develop and treat the disease. Moreover, in patients with acute meningitis, lymphocyte responsiveness is markedly depressed (Murray *et al.*, Medical Microbiology, 4th ed., 2002, page 262).

Therefore, in view of the lack of support in the art and specification for vaccines for the treatment of neisserial disease, it would require undue experimentation on the part of the skilled artisan to make and use the vaccine as claimed; therefore the full scope of the claims is not enabled.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6-10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is rendered vague and indefinite by the phrase "vaccine for the treatment of." Vaccines are used to provide protective immunity, not for the treatment of disease.

Conclusion

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian J. Gangle whose telephone number is (571) 272-1181. The examiner can normally be reached on M-F 7-3:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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